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Ambient Water Quality Criteria: Chlordane

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CHLORDANE

Ambient Water Quality Criteria

Criteria and Standards Division
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CRITERION DOCUMENT

CHLORDANE

CRITERIA

Aquatic Life

For chlordane the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.024 µg/l as a 24-hour average and the concentration should not exceed 0.36 µg/l at any time.

For chlordane the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.0091 µg/l as a 24-hour average and the concentration should not exceed 0.18 µg/l at any time.

Human Health

For the maximum protection of human health from the potential carcinogenic effects of exposure to chlordane through ingestion of water and contaminated aquatic organisms, the ambient water concentration is zero. Concentrations of chlordane estimated to result in additional lifetime cancer risks ranging from no additional risk to an additional risk of 1 in 100,000 are presented in the Criterion Formulation section of this document. The Agency is considering setting criteria at an interim target risk level in the range of 10^{-5}, 10^{-6}, or 10^{-7} with corresponding criteria of 1.2 ng/l, 0.12 ng/l, and 0.012 ng/l, respectively.

BIBLIOGRAPHIC INFORMATION

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Section 304(a) of the Clean Water Act (33 U.S.C. 1314(a)), requires EPA to publish and periodically update water quality criteria. These criteria are to reflect the latest scientific knowledge on the identifiable effects of pollutants on public health and welfare, aquatic life, and recreation. This report presents water quality criteria for the insecticide, chlordane. It presents concentration criteria for the protection of fresh water and saltwater aquatic life. It presents 'safe' concentrations for humans, and in the case of suspect or proven carcinogens, gives various levels of incremental cancer risk. A section 304(a) water quality criterion is a qualitative or quantitative estimate of the concentration of a water constituent or pollutant in ambient waters which, when not exceeded, will ensure a water quality sufficient to protect a specified water use. Under the Act a criterion is a scientific entity, based solely on data and scientific judgment. It does not reflect considerations of economic or technological feasibility nor is it a water quality standard and , ...

KEYWORDS: *Water quality, *Toxicology, *Chlordan, *Water pollution effects(Humans), *Water pollution effects(Animals), *Toxic substances, *Methanoindene/hexachloro-octahydro, *Methanoindan/octachloro-tetrahydro.

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Introduction

Chlordane is a broad spectrum insecticide of the group of polycyclic chlorinated hydrocarbons called cyclodiene insecticides. Chlordane has been used extensively over the past 30 years for termite control, as an insecticide for homes and gardens, and as a control for soil insects during the production of crops such as corn. Production of chlordane in the United States approached 10,000 metric tons per year in 1974 (41 FR 7558; February 19, 1976). Both the uses and the production volume of chlordane have decreased extensively since the issuance of a registration suspension notice for all food crops and home and garden uses of chlordane by the U.S. Environmental Protection Agency (40 FR 34456; December 24, 1975). However, significant commercial use of chlordane for termite control continues. In addition, under the terms of a recent settlement which terminated chlordane registration cancellation proceedings, chlordane will be permitted for limited usage through 1980 as an agricultural insecticide (43 FR 12372; March 24, 1978).

Pure chlordane is a pale yellow liquid having the molecular formula $C_{10}H_6Cl_8$ and a molecular weight of 409.8 (Windholz, 1976; Whetstone, 1972). The chemical name for chlordane is 1,2,4,5,6,7,8,8-octachloro-2,3,3a,4,7,7a-hexahydro-4,7-methanoindene (Windholz, 1976). Pure chlordane is composed of a mixture of stereoisomers, with the cis and trans forms predominating and referred to as alpha and gamma isomers, respectively (Brooks, 1974). Pure chlordane is soluble

in water at concentrations which have been shown to be toxic to aquatic organisms. Brooks (1974) reported the solubility of chlordane in water to be approximately 9 µg/l at 25 degrees C.

Chlordane is produced by the chlorination of chlordene which, in turn, is a product of hexachlorocyclopentadiene and cyclopentadiene (Whetstone, 1972). Oxychlordane, a metabolic product of chlordane produced in both plants and animals, has been demonstrated to be more toxic than the parent compound and to persist in the adipose tissue of mammals (Street and Blau, 1972; Polen, et al. 1971; Dorough, et al. 1973; Mastri, et al. 1969).

Technical grade chlordane is a mixture of various chlorinated hydrocarbons with a typical composition of approximately 24 percent trans (gamma) chlordane, 19 percent cis (alpha) chlordane, 10 percent heptachlor, 21.5 percent chlordene isomers, 7 percent nonachlor and 18.5 percent closely related chlorinated hydrocarbon compounds (Velsicol Chemical Corp., 1971). Technical chlordane is a viscous, amber-colored liquid with a cedar-like odor and is relatively non-volatile, having a vapor pressure of 1 x 10^{-5} mm Hg at 25 degrees C; it is soluble in water at toxic concentrations (150 to 220 µg/l at 22 degrees C) and has a density greater than that of water, approximately 1.65 g/ml at 16 degrees C (Metcalf, 1955; Whetstone, 1972; Cardwell, et al. 1977).

Chlordane has been detected at various concentrations in ambient water, finished drinking water, rainwater, and soils. Chlordane is readily soluble in natural fats and fat soluble substances (Brooks, 1974). As a result, it accumulates

in the tissues of organisms, particularly in the adipose tissue or body fat. Chlordane has been found in plankton, earthworms, shellfish, fish, birds, bird eggs, and man and several other mammals.

Chlordane has been demonstrated to be highly toxic to aquatic organisms, to bioconcentrate in many aquatic species, and to persist for prolonged periods in the environment. It is toxic to avian and mammalian species and exhibits carcinogenic activity in mice. Thus, chlordane in water is a hazard to both aquatic and terrestrial life.

REFERENCES

Brooks, G.T. 1974. Chlorinated insecticides. CRC Press, Cleveland, Ohio.

Cardwell, R.D., et al. 1977. Acute and chronic toxicity of chlordane to fish and invertebrates. EPA-600/3-77-019. U.S. Environ. Prot. Agency.

Dorough, H.W., et al. 1973. Chlordane residues in milk and fat of cows fed HCS 3260 (high purity chlordane) in the diet. Bull. Environ. Contam. Toxicol. 10: 208.

Mastri, C., et al. 1969. Unpublished data. In 1970 evaluation of some pesticide residues in food. Food Agric. Org. United Nations/World Health Org.

Metcalf, R.L. 1955. Organic insecticides. Interscience Publishers, Inc., New York.

Polen, P.B., et al. 1971. Characterization of oxychlordane, animal metabolite of chlordane. Bull. Environ. Contam. Toxicol. 5: 521.

Street, J.E., and S.E. Blau. 1972. Oxychlordane: accumulation in rat adipose tissue on feeding chlordane isomers or technical chlordane. Jour. Agric. Food Chem. 20: 395.

Velsicol Chemical Corp. 1971. Standard for technical chlordane. Chicago.

Whetstone, R.R. 1972. Kirk-Othmer encyclopedia of chemical technology. John Wiley and Sons, Inc., New York.

Windholz, M. 1976. The Merck Index. Merck and Co. Inc., Rahway, N.J.

AQUATIC LIFE TOXICOLOGY*

FRESHWATER ORGANISMS

Introduction

Although chlordane has been used as an insecticide for many years, our knowledge of its toxicity to aquatic life is less complete than for other chlorinated hydrocarbon insecticides such as DDT and dieldrin. Early studies (Katz, 1961; Henderson, et al. 1959) using static test procedures showed it to be substantially less toxic than endrin, dieldrin, DDT and toxaphene. Perhaps as a result, few additional data appear in the literature until the 1970's.

Chronic data were published recently, but dealt with only a few species. Data for bioconcentration likewise is mostly of recent origin. There are, however, virtually no bioconcentration data for freshwater fish.

The effect on aquatic plants is not known but probably is not important because this chemical is formulated as an insecticide and not as a herbicide.

Acute Toxicity

In Table 1 it is shown that 18 LC50 values are available for ten species of fish. Because all but one species were tested for 96 hours, correction for test duration is needed in only one instance. Three of the 18 LC50 values are from

*The reader is referred to the Guidelines for Deriving Water Quality Criteria for the Protection of Aquatic Life [43 FR 21506 (May 18, 1978) and 43 FR 29028 (July 5, 1978)] and the Methodology Document in order to better understand the following discussion and recommendation. The following tables contain the appropriate data that were found in the literature, and at the bottom of each table are the calculations for deriving various measures of toxicity as described in the Guidelines.

flow-through tests and the rest are from static tests. Since chlordane is not highly water soluble, one might suspect that static tests would underestimate toxicity. Data available for fathead minnows in static and flow-through tests in Table 1 show the flow-through result to be at least 30 percent lower than the static. After the data from static tests are adjusted for test conditions, the LC50 values are more closely clustered. The flow-through test for bluegills also yielded a lower LC50 than the static tests. As was observed with the data for fathead minnows above, when static data are adjusted for test conditions, the resultant values are closer to the flow-through data.

One of the five LC50 values for salmonids is about 7 percent of the geometric mean for all species, whereas the other four are from 40 to 50 percent of the mean. The geometric mean is influenced more by the two high values of 514 (Ludemann and Neumann, 1960) and 437 µg/l (Clemens and Sneed, 1959) than by the two lowest values of 4 (Mehrle, et al. 1974) and 12 µg/l (Henderson, et al. 1959). The other 14 LC50 values are between 40 percent of the geometric mean and the mean value. Because nothing sufficient was found to question the validity of these four values, there was no reason to delete them from the data base.

The 14 mid-range LC50 values display less species variability than that which occurs for some other chlorinated hydrocarbon pesticides. When the geometric mean of all values in Table 1 is divided by the sensitivity factor, 3.9, the LC50 calculated to be equal or less than the LC50

for 95 percent of species is higher than 2 values in the table. This suggests a very reasonable fit of the data to the procedures in the Guidelines. The Final Fish Acute Value is 16 µg/l.

The data base for invertebrates (Table 2) contains seven data points for five species, four of which represent rather different decapods and insects. In addition, Table 6 contains a 96-hour LC50 for Daphnia magna (Cardwell, et al. 1977) which was excluded from Table 2 since the standard duration for acute tests with daphnids is 48 hours. We can see from that test, however, that Daphnia magna is less sensitive than other invertebrate species (Table 2).

Flow-through and static tests on the freshwater shrimp were conducted (Sanders, 1972), showing 2.5 times greater toxicity in flow-through tests. This result supports the need to adjust static test values before combining them with flow-through data. The adjustment for static conditions, unmeasured concentrations, and a 24-hour instead of a 96-hour test were made, the result for the freshwater shrimp was an LC50 of 3 µg/l (Naqvi and Ferguson, 1970). This was almost the same value as Sanders (1972) obtained for the same species in a flow-through 96-hour test. However, the adjustment of Sanders' static test data did not result in the same estimate.

The range of species sensitivity (the highest LC50 divided by the lowest) displayed in Table 2 is 15.4. When the geometric mean of the data is divided by the sensitivity factor (21), the estimated value (at or below the LC50)

for 95 percent of all species is 0.36 µg/l, approximately one-sixth of the lowest LC50 in Table 2. In view of the wide diversity of invertebrate physiology and the data base of 5 species, the sensitivity factor does not seem to be inappropriate.

Since the Final Invertebrate Acute Value (Table 2) of 0.36 µg/l is lower than the Final Fish Acute Value of 16 µg/l (Table 1), the Final Acute Value for freshwater aquatic life is 0.36 µg/l.

Chronic Toxicity

One chronic test with bluegills was found (Table 3). A comparison of the 96-hour LC50 from this report shows that the acute toxicity value is about 37 times greater than the value for chronic toxicity. The chronic value divided by the sensitivity factor (6.7) from the Guidelines gives a 95 percent species protection concentration of 0.24 µg/l. A different method of estimating the same value is obtained by multiplying the Final Fish Acute Value by the application factor calculated from the bluegill data. This estimate is 0.85 µg/l, about three times larger. Since only one chronic data point is available, no indication of the range of sensitivity for chronic toxicity is available. However, the above comparison suggests the Guideline sensitivity factor is reasonable for fish chronic toxicity. Since bluegills are among the less sensitive of the species acutely tested (Table 1), reduction of the bluegill chronic data by the sensitivity factor would appear to be necessary to protect more sensitive species from chronic toxicity. The

Final Fish Chronic Value is the lowest of the three estimates in Table 3, or 0.24 µg/l.

Chronic data are available for Daphnia magna with a chronic value of 16.2 µg/l (Table 4). The LC50 value from the same work (Cardwell, et al. 1977) is a 96-hour value of 28.4 µg/l and, as noted previously, is in Table 6. As with the fish, the range of sensitivity for invertebrate species cannot be determined from chronic data, but may be inferred from acute data (Table 2). Since Daphnia magna are among the less sensitive invertebrates in acute tests (Table 2), an adjustment is clearly needed. The Final Invertebrate Chronic Value is 3.2 µg/l, a value obviously underprotective since it exceeds three of the seven LC50 values in Table 2 for acute toxicity to invertebrates.

Since the value to protect against chronic toxicity is the lowest of the values derived from chronic data for fish, invertebrates, plants and the Residue Limited Toxicant Concentration (RLTC), protection of invertebrates may be provided by lower values indicated by data in these other areas. By referring back to Table 3, it can be seen that the Final Fish Chronic Value is 0.24 µg/l. Later we will see that the RLTC is 0.024 µg/l and that there are no data for plants. Since for Daphnia magna (Cardwell, et al. 1977) the difference between the acute and chronic values is small, the use of the RLTC or the Final Fish Chronic Value would seem to be adequately protective of invertebrates. There are no data in Table 6 to contradict that conclusion.

Plant Effects

No data for plant toxicity were found.

Residues

Table 5 contains equilibrium bioconcentration data on chlordane and closely related chemicals for two invertebrates. The arithmetic mean of all the data is 5,400. The substantially higher bioconcentration factors for Oedegonium sp. and Physa sp. (Sanborn, et al. 1976) in Table 6 were not used in the RLTC calculations because test conditions suggest that these high values may not reflect true readings of actual exposures. Data, however, from the same work for mosquito larva are about 6,000, a value in line with the data in Table 5 for other invertebrates. Use of the algae and snail data would lower the RLTC by a factor of about 20. Since water concentrations were only measured at the end of the 33-day test it may be that water concentrations, and hence exposures, were not uniform with time. It may mean also that these higher bioconcentration factors occurred when water concentrations were high but not measured, and that they remained after the water concentrations had decreased and been measured. In such a case, the calculated BCF would be too high.

A residue limit for consumers of aquatic life, established by the FDA limit for chlordane in animal feed of 0.1 mg/kg, was used to calculate the RLTC. Fish meal is used in domestic animal feed and so seems applicable here. Furthermore, various aquatic animals are eaten by turtles, frogs, ducks and some fish which are then eaten by man. The animal feed level

would appear applicable for this situation as well. Therefore, the FDA animal feed level of 0.1 mg/kg, divided by the bioconcentration factor of 4,200, gives a RLTC of 0.024 µg/l.

Of the four values (the Final Fish Chronic Value (0.24 µg/l), Final Invertebrate Chronic Value (3.2 µg/l), Final Plant Value (no data) and the RLTC (0.024 µg/l)), the RLTC of 0.024 µg/l is the lowest and becomes the Final Chronic Value.

Miscellaneous

Table 6 contains no data that would appear to alter the selection of 0.024 µg/l for the Final Chronic Value, except for the work of Sanborn, et al. (1976) which, as discussed earlier, needs further experimental verification for use at this time.

CRITERION FORMULATION

Freshwater - Aquatic Life

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value = 16 µg/l

Final Invertebrate Acute Value = 0.36 µg/l

Final Acute Value = 0.36 µg/l

Final Fish Chronic Value = 0.24 µg/l

Final Invertebrate Chronic Value = 3.2 µg/l

Final Plant Value = not available

Residue Limited Toxicant Concentration = 0.024 µg/l

Final Chronic Value = 0.024 µg/l

0.44 x Final Acute Value = 0.16 µg/l

The maximum concentration of chlordane is the Final Acute Value of 0.36 µg/l and the 24-hour average concentration is the Final Chronic Value of 0.024 µg/l. No important adverse effects on freshwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For chlordane the criterion to protect freshwater aquatic life as derived using the Guidelines is 0.024 µg/l as a 24-hour average and the concentration should not exceed 0.36 µg/l at any time.

Table 1. Freshwater fish acute values for chlordane

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Coho salmon (age 0), Oncorhynchus kisutch	S	U	Chlordane 100% A.I.	96	56	31	Katz, 1961
Chinook salmon (age 0), Oncorhynchus tshawytscha	S	U	Chlordane 100% A.I.	96	57	31	Katz, 1961
Rainbow trout (age 0), Salmo gairdneri	S	U	Chlordane 100% A.I.	96	44	24	Katz, 1961
Rainbow trout, Salmo gairdneri	S	U	Technical chlordane	96	47	26	Mehrle, et al. 1974
Rainbow trout, Salmo gairdneri	S	U	Technical chlordane	96	8	4	Mehrle, et al. 1974
Brook trout (adult), Salvelinus fontinalis	FT	M	Technical chlordane	96	45	45	Cardwell, et al. 1977
Goldfish, Carrasius auratas	S	U	Chlordane 100% A.I.	96	82	45	Henderson, et al. 1959
Carp (fingerling), Cyprinus carpio	S	U	Chlordane	48	1,160	514	Ludemann Neumann, 1960
Fathead minnow, Pimephales promelas	S	U	Chlordane 100% A.I.	96	52	28	Henderson, et al. 1959
Fathead minnow, Pimephales promelas	S	U	Chlordane 100% A.I.	96	69	38	Henderson, et al. 1959
Fathead minnow (juvenile), Pimephales promelas	FT	M	Technical chlordane	96	37	37	Cardwell, et al. 1977
Channel catfish, Ictalurus punctatus	S	U	Chlordane	96	800***	437	Clemens & Sneed, 1959
Guppy, Poecilia reticulata	S	U	Chlordane 100% A.I.	96	190	104	Henderson, et al. 1959
Bluegill, Lepomis macrochirus	S	U	Chlordane 100% A.I.	96	22	12	Henderson, et al. 1959
Bluegill, Lepomis macrochirus	S	U	Technical chlordane	96	77	42	Macek, et al. 1969

Table 1. (Continued)

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Bluegill, Lepomis macrochirus	S	U	Technical chlordane	96	77	42	Macek, et al. 1969
Bluegill, Lepomis macrochirus	S	U	Technical chlordane	96	85	47	Macek, et al. 1969
Bluegill (juvenile), Lepomis macrochirus	FT	M	Technical chlordane	96	59	59	Cardwell, et al. 1977

* S = static, FT = flow-through

** U = unmeasured, M = measured

*** Authors reported 500 ppm by volume

Geometric mean of adjusted acute values = 61.3 µg/l $\frac{61.3}{3.9}$ = 16 µg/l

Lowest value from a flow-through test with measured concentrations = 37 µg/l

Table 2. Freshwater invertebrate acute values for chlordane

Organism	Bioassay Method*	Test Conc.**	Chemical Description	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Scud, Gammarus fasciatus	S	U	Technical chlordane	96	40	34.0	Sanders, 1972
Scud, Gammarus lacustris	S	U	Technical chlordane	96	26	22.0	Sanders, 1969
Freshwater shrimp, Palaemonetes kadiakensis	S	U	Technical chlordane	24	13.6	3.0	Naqvi & Ferguson, 1970
Freshwater shrimp, Palaemonetes kadiakensis	S	U	Technical chlordane	96	10	8.5	Sanders, 1972
Freshwater shrimp, Palaemonetes kadiakensis	FT	U	Technical chlordane	96	4	3.1	Sanders, 1972
Stonefly, Pteronarcys californica	S	U	Technical chlordane	96	15	12.7	Sanders & Cope, 1968
Midge (larva), Chironomus plumosus	S	U	Chlordane	24	10	2.2	Ludemann & Neumann, 1962

* S = static, FT = flow-through

** U = unmeasured

Geometric mean of adjusted acute values = 7.57 µg/l $\frac{7.57}{21}$ = 0.36 µg/l

Table 3. Freshwater fish chronic values for chlordane (Cardwell, et al. 1977)

Organism	Test*	Limits (ug/l)	Chronic Value (ug/l)
Bluegill, *Lepomis macrochirus*	LC	1.22-2.20	1.6

* LC = life cycle or partial life cycle

Geometric mean of chronic values = 1.6 µg/l $\quad \frac{1.6}{6.7} = 0.24$ µg/l

Lowest chronic value = 1.6 µg/l

Application Factor Values

Species	96-hr LC50 (µg/l)	MATC (µg/l)	AF
Bluegill, *Lepomis macrochirus*	59	1.22-2.20	0.028

Geometric mean AF = 0.028 $\qquad$ Geometric mean LC50 = 59 µg/l

$$0.028 \sqrt{59 \text{ µg/l} \times 15.7 \text{ µg/l}} = 0.85 \text{ µg/l}$$

Table 4. Freshwater invertebrate chronic values for chlordane (Cardwell, et al. 1977)

Organism	Test*	Limits (ug/l)	Chronic Value (ug/l)
Cladoceran, Daphnia magna	LC	12.1-21.6	16.2

* LC = life cycle or partial life cycle

Geometric mean of chronic values = 16.2 µg/l $\frac{16.2}{5.1}$ = 3.2 µg/l

Lowest chronic value = 16.2 µg/l

Table 5. Freshwater residues for chlordane (Cardwell, et al. 1977)

Organism	Bioconcentration Factor*	Time (days)
Cladoceran, Daphnia magna	900 (Heptachlor)	7
Cladoceran, Daphnia magna	2,500 (Chlordenes)	7
Cladoceran, Daphnia magna	6,000 (Chlordanes)	7
Cladoceran, Daphnia magna	8,900 (Nonachlors)	7
Scud, Hyaliela azteca	2,200 (Heptachlor)	65
Scud, Hyaliela azteca	5,000 (Chlordenes)	65
Scud, Hyaliela azteca	7,400 (Chlordanes)	65
Scud, Hyaliela azteca	10,400 (Nonachlors)	65

Maximum Permissible Tissue Concentration

Organism	Action Level or Effect	Concentration (mg/kg)	Reference
Domestic animals	animal feed	0.1	FDA Admin. Guideline 7426.04, 1977

* Arithmetic mean of 8 or 16 bioconcentration factors, values adjusted for wet weights

Geometric mean bioconcentration factor for all species = 4,200

Lowest residue concentration = 0.1 mg/kg

$\frac{0.1}{4,200}$ = 0.000024 mg/kg or 0.024 µg/l

Table 6. Other freshwater data for chlordane

Organism	Test Duration	Effect	Result ug/l	Reference
Alga, *Oedegonium cardiacum*	33 days	Bioconcentration of Chlordene: 11,000	Model ecosystem	Lu, et al. 1975
Alga, *Oedegonium sp.*	33 days	Bioconcentration of Chlordane: 98,000	Model ecosystem	Sanborn, et al. 1976
Aquatic worm, *Branchiura sowerbyi*	72 hrs	LC100	500	Naqvi, 1973
Aquatic worm, *Tubifex tubifex*	96 hrs	LC100	10,000	Ludemann & Newmann, 1962
Snail, *Physa sp.*	33 days	Bioconcentration of Chlordene: 53,000	Model ecosystem	Lu, et al. 1975
Snail, *Physa sp.*	33 days	Bioconcentration of Chlordane: 133,000	Model ecosystem	Sanborn, et al. 1976
Cladoceran, *Daphnia pulex*	24 hrs	Bioconcentration of Chlordane: 2,400*	0.5 (static)	Moore, et al. 1977
Cladoceran, *Daphnia magna*	96 hrs	LC50	28.4	Cardwell, et al. 1977
Scud, *Hyallela azteca*	168 hrs	LC50	97.1	Cardwell, et al. 1977
Scud, *Hyallela azteca*	65 days	Reduced growth and survival	11.5	Cardwell, et al. 1977
Freshwater shrimp, *P. kadiakensis*	120 hrs	LC50	2.5	Sanders, 1972
Midge, *Chironomus* No. 51	25 days	Larval mortality	1.7	Cardwell, et al. 1977
Mosquito (larva), *Culex pipiens*	33 days	Bioconcentration of Chlordene: 2,000	Model ecosystem	Lu, et al. 1975
Mosquito (larva), *Culex sp.*	33 days	Bioconcentration of Chlordane: 6,000	Model ecosystem	Sanborn, et al. 1976
Rainbow trout, *Salmo gairdneri*	24 hrs	LC100	500	Mayhew, 1955

Table 6. (Continued)

Organism	Test Duration	Effect	Result ug/l	Reference
Rainbow trout, Salmo gairdneri	5 hrs	Death or distress	100	Applegate, et al. 1957
Rainbow trout, Salmo gairdneri	24 hrs	LC100	1,000	Ludemann & Neumann, 1961
Brook trout, Salvelinus fontinalis	13 mos	Reduced embryo viability	0.32	Cardwell, et al. 1977
Northern pike, Esox lucius	24 hrs	LC100	50	Ludemann & Neumann, 1961
Goldfish, Carassius auratus	96 hrs	Bioconcentration of Chlordane: 160	3.4 (static)	Moore, et al. 1977
Carp (embryo), Cyprinus carpio	96 hrs	Mortality	5,000	Malone & Blaylock, 1970
Carp (embryo), Cyprinus carpio	91 hrs	Accelerated development	1.0	Malone & Blaylock, 1970
Mosquitofish, Gambusia affinis	33 days	Bioconcentration of Chlordene: 1,000	Model ecosystem	Lu, et al. 1975
Mosquitofish, Gambusia affinis	33 days	Bioconcentration of Chlordane: 8,000	Model ecosystem	Sanborn, et al. 1976
Green sunfish, Lepomis cyanellus	15 min	Avoidance	5,000	Summerfelt & Lewis, 1967
Largemouth bass, Micropterus salmoides	33 hrs	Increased opercular rate	30	Morgan, 1975
Toad (tadpole), Bufo bufo	48 hrs	LC100	2,000	Ludemann & Neumann, 1962

* Adjusted for wet weight

SALTWATER ORGANISMS

Introduction

The chlordane data base for saltwater organisms is smaller than for freshwater and the data are insufficient to determine the importance of salinity, temperature, or other water quality factors to the toxicity of this insecticide. The toxicities of major chemicals in technical chlordane have not been studied and relative toxicity of each chemical responsible for chlordane's effects has not been identified.

Acute Toxicity

Five species of saltwater fish have been tested for the acute effects of chlordane (Table 7). In flow-through exposure, the 96-hour LC50's for three species ranged from 6.4 to 24.5 µg/l (Korn and Earnest, 1974; Parrish, et al. 1976, 1978). Two LC50's for stickleback from static tests and unmeasured concentrations are 90 and 160 µg/l. After adjustment for test conditions, these LC50 values are three or more times higher than other species, suggesting true differences in species sensitivity. The adjusted LC50 values differ by a factor of more than 25 times. When the geometric mean is divided by the sensitivity factor from the Guidelines, a value of 3.2 µg/l is calculated. Since this value is close to the lowest value in the table and there are data for only five species, the adjustment seems reasonable. The Final Fish Acute Value is 3.2 µg/l, a value expected to be equal to or lower than LC50 value for 95 percent of all saltwater fish species.

Invertebrate LC50 values in Table 8 range from 0.4 to 480 µg/l before adjustments and from 0.4 to 186 µg/l after adjustments are made for test conditions. The pink shrimp is over five times more sensitive than the second most sensitive species. The crabs are over 20 times more tolerant than the second most insensitive species and about 400 times more tolerant than the most sensitive species. Caldwell (1977) observed substantial mortality in adult crabs between 4 and 90 days exposure indicating a higher toxicity than is reflected in the Butler data (1963). The geometric mean divided by the sensitivity factor (49) gives an LC50 value of 0.18 µg/l. This value is about two times lower than the lowest value in Table 2. Since there are data for only four species, the calculated Final Invertebrate Acute Value of 0.18 µg/l seems reasonable. This also becomes the Final Acute Value since the Final Fish Acute Value (3.2 µg/l) is higher.

Chronic Toxicity

Chlordane was chronically toxic to the estuarine sheepshead minnow (Table 9) in an entire life-cycle exposure at $\geq$ 0.8 µg/l (Parrish, et al. 1978). Survival of juveniles was reduced at 18 µg/l, and their survival through adulthood was reduced at 2.8 µg/l (Parrish, et al. 1978). Reproduction of exposed adult fish was not impaired but hatching of embryos was decreased at 0.8 µg/l and juvenile survival decreased at 1.7 µg/l. No significant effects were observed on survival, growth, or reproduction at a chlordane concentration of 0.5 µg/l. The concentration not affecting sheepshead minnows

in this chronic exposure was 0.04 of the 96-hour LC50. In an embryo-larval test, 17 µg/l was lethal to fry, but 7.1 µg/l was not (Parrish, et al. 1976). Usually, results of embryo-larval tests can be used to predict (within a factor of two) results of life-cycle tests. Chlordane, because of its effects on adult fish and their progeny, is an obvious exception to this general relationship. Of the three estimates of chronic toxicity in Table 9, two are not different, given the variability of the data base, and the third is about twice as high. The lower of the three, the geometric mean adjusted for sensitivity, is used as the Final Fish Chronic Value, 0.28 µg/l.

No life-cycle chronic tests with invertebrates were found. Extended exposure of Dungeness crab zoeae and adults by Caldwell (1977) demonstrated that acute tests can underestimate the chronic toxicity of chlordane (Table 12). The 96-hour LC50 of chlordane to crab zoeae was greater than 10 µg/l. Moulting was not affected at 9.15 µg/l, and this concentration was lethal to 50 percent after 37 days of exposure. Survival and moulting were unaffected in chlordane concentrations of 0.015 µg/l. The 96-hour LC50 for adults was 220 µg/l. Most adult crabs died after a 90-day continuous exposure to 10 µg/l, but survival in 1 µg/l did not differ from controls. These results indicate a large difference between the 96-hour LC50 and the 90-day LC50.

Plant Effects

Information on the sensitivity of aquatic plants, including algae and rooted vascular plants, is limited to one

test using a 4-hour exposure of a mixed phytoplankton community (Table 10).

Residues

Equilibrium bioconcentration factors for the sheepshead minnow ranged from 6,580 to 16,035 with an average value of 12,000 (Table 11). The acceptable residue level is the same as the one used for freshwater aquatic life discussed above. That value divided by the average bioconcentration factor gives a Residue Limited Toxicant Concentration (RLTC) of 0.0091 µg/l.

Of the four components used to establish the Final Chronic Value (Final Fish Chronic Value, 2.8 µg/l, Final Invertebrate Chronic Value, no data, Final Plant Value, 1,000 µg/l; and the RLTC, 0.0091 µg/l), the RLTC is lowest, and that concentration becomes the Final Chronic Value.

Miscellaneous

No other data from Table 12 suggest any more sensitive effects.

CRITERION FORMULATION

Saltwater - Aquatic Life

Summary of Available Data

The concentrations below have been rounded to two significant figures.

Final Fish Acute Value = 3.2 µg/l

Final Invertebrate Acute Value = 0.18 µg/l

Final Acute Value = 0.18 µg/l

Final Fish Chronic Value = 0.28 µg/l

Final Invertebrate Chronic Value = not available

Final Plant Value = 1,000 µg/l

Residue Limited Toxicant Concentration = 0.0091 µg/l

Final Chronic Value = 0.0091 µg/l

0.44 x Final Acute Value = 0.79 µg/l

The maximum concentration of chlordane is the Final Acute Value of 0.18 µg/l and the 24-hour average concentration is the Final Chronic Value of 0.0091 µg/l. No important adverse effects on saltwater aquatic organisms have been reported to be caused by concentrations lower than the 24-hour average concentration.

CRITERION: For chlordane the criterion to protect saltwater aquatic life as derived using the Guidelines is 0.0091 µg/l as a 24-hour average and the concentration should not exceed 0.18 µg/l at any time.

Table 7. Marine fish acute values for chlordane

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	Reference
Sheepshead minnow, Cyprinodon variegatus	FT	M	96	24.5	24.5	Parrish, et al. 1976
Sheepshead minnow, Cyprinodon variegatus	FT	M	96	12.5	12.5	Parrish, et al. 1978
Threespine stickleback (adult), Gasterosteus aculeatus	S	U	96	90	49.2	Katz, 1961
Threespine stickleback (adult), Gasterosteus aculeatus	S	U	96	160	87.47	Katz, 1961
Striped bass, Morone saxatilis	FT	U	96	11.8	9.086	Korn & Earnest, 1974
Pinfish, Lagodon rhomboides	FT	M	96	6.4	6.4	Parrish, et al. 1976
White mullet (juvenile), Mugil curema	FT	U	48	5.5	3.43	Butler, 1963

* S = static, FT = flow-through

** U = unmeasured, M = measured

Geometric mean of adjusted values = 11.8 µg/l $\frac{11.8}{3.7}$ = 3.2 µg/l

Lowest value from a flow-through test with measured concentrations = 6.4 µg/l

Table 8. Marine invertebrate acute values for chlordane

Organism	Bioassay Method*	Test Conc.**	Time (hrs)	LC50 (ug/l)	Adjusted LC50 (ug/l)	References
Eastern oyster (yearling), Crassostrea virginica	S	U	24	10.0***	2.2	Butler, et al. 1960
Eastern oyster, Crassostrea virginica	FT	U	96	7.0***	5.39	Butler, 1963
Eastern oyster, Crassostrea virginica	FT	U	96	10.0***	7.7	Butler, 1963
Eastern oyster, Crassostrea virginica	FT	M	96	6.2***	6.2	Parrish, et al. 1976
Brown shrimp (adult), Penaeus aztecus	FT	U	48	4.4***	1.46	Butler, 1963
Pink shrimp, Penaeus duorarum	FT	M	96	0.4	0.4	Parrish, et al. 1976
Grass shrimp, Palaemontes pugio	FT	M	96	4.8	4.8	Parrish, et al. 1976
Blue crab (juvenile), Callinectes sapidus	FT	U	48	480.0***	158.9	Butler, 1963
Dungeness crab (adult), Cancer magister	S	U	96	220.0	186.0	Caldwell, 1977

* S = static, FT = flow-through

** U = unmeasured, M = measured

*** EC50: Decreased shell growth of oyster; or loss of equilibrium of brown shrimp or blue crabs.

Geometric mean of adjusted values = 8.598 µg/l $\frac{8.598}{49}$ = 0.18 µg/l

Lowest value from a flow-through test with measured concentrations = 0.4 µg/l

Table 9. Marine fish chronic values for chlordane

Organism	Test*	Limits (ug/l)	Chronic Value (ug/l)	Reference
Sheepshead minnow, Cyprinodon variegatus	E-L	7.1-17	5.49	Parrish, et al. 1976
Sheepshead minnow, Cyprinodon variegatus	LC	0.5- 0.8	0.63	Parrish, et al. 1978

* LC = life cycle or partial life cycle, E-L = embryo-larval

Geometric mean of chronic values = 1.863 µg/l $\frac{1.86}{6.7}$ = 0.28 µg/l

Lowest chronic value = 0.63 µg/l

Application Factor Values

Species	96-hr LC50 (µg/l)	MATC (µg/l)	AF	Reference
Sheepshead minnow, Cyprinodon variegatus	12.5	0.5-0.8	0.0489	Parrish, et al. 1978

Geometric Mean AF = 0.0489

Geometric mean LC50 = 12.5 µg/l

$0.0489 \sqrt{12.5 \text{ µg/l} \times 3.89 \text{ µg/l}} = 0.31 \text{ µg/l}$

Table 10. Marine plant effects for chlordane (Butler, 1963)

Organism	Effect	Concentration (ug/l)
Natural phytoplankton community	94% decrease in productivity during 4-hr exposure	1,000

Lowest plant value = 1,000 µg/l

Table 11, Marine residues for chlordane

Organism	Bioconcentration Factor	Time (days)	Reference
Sheepshead minnow (juvenile), Cyprinodon variegatus	10,339	28	Parrish, et al. 1976
Sheepshead minnow (adult), Cyprinodon variegatus	16,035	189	Parrish, et al. 1978
Sheepshead minnow (juvenile), Cyprinodon variegatus	15,311	28	Parrish, et al. 1978
Sheepshead minnow (juvenile), Cyprinodon variegatus	6,580	28	Goodman, et al. 1978

	Maximum Permissible Tissue Concentration		
Organism	Action Level or Effect	Concentration (mg/kg)	Reference
Domestic animals	animal feed	0.1	U.S. FDA Admin. Guideline - 7426.04, 1977

Geometric mean bioconcentration factor = 11,000

Lowest residue concentration = 0.1 mg/kg

$\frac{0.1}{11,000}$ = 0.0000091 mg/kg or 0.0091 ug/l

Table 12. Other marine data for chlordane

Organism	Test Duration	Effect	Result (ug/l)	Reference
Eastern oyster, *Crassostrea virginica*	96 hrs	Bioconcentration factor 5,522	--	Parrish, et al. 1976
Pink shrimp, *Penaeus duorarum*	96 hrs	Bioconcentration factor 4,564	--	Parrish, et al. 1976
Grass shrimp, *Palaemonetes pugio*	96 hrs	Bioconcentration factor 2,117	--	Parrish, et al. 1976
Sheepshead minnow, *Cyprinodon variegatus*	96 hrs	Bioconcentration factor 15,250	--	Parrish, et al. 1976
Sheepshead minnow, *Cyprinodon variegatus*	96 hrs	Bioconcentration factor 12,900	--	Schimmel, et al. 1976a
Pinfish, *Lagodon rhomboides*	96 hrs	Bioconcentration factor 6,227	--	Parrish, et al. 1976
Spot, *Leiostomus xanthurus*	96 hrs	Bioconcentration factor 9,250	--	Schimmel, et al. 1976a
Spot, *Leiostomus xanthurus*	72 hrs	Bioconcentration factor 4,600	--	Schimmel, et al. 1976b
Dungeness crab (zoeae), *Cancer magister*	96 hrs	LC50	10	Caldwell, 1977
Dungeness crab, *Cancer magister*	>70 days	50% larval mortality on 37 day, retardation of molting	0.15	Caldwell, 1977
Dungeness crab, *Cancer magister*	>70 days	No effect	0.015	Caldwell, 1977
Dungeness crab, *Cancer magister*	90 days	Survival not affected	1	Caldwell, 1977

REFERENCES

Applegate, V.C., et al. 1957. Toxicity of 4,346 chemicals to larval lampreys and fishes. U.S. Dep. Inter. Fish Wildl. Serv. Rep. 207.

Butler, P.A. 1963. Commercial fisheries investigations. In Pesticide and wildlife studies. A review of Fish and Wildlife Service investigations during 1961 and 1962. U.S. Fish Wildl. Serv. Circ. 167: 11.

Butler, P.A., et al. 1960. Effect of pesticides on oysters. Proc. Shell Fish Assoc. 51: 23.

Caldwell, R.S. 1977. Biological effects of pesticides on the Dungeness crab. EPA 600/3-77-131: 1. U.S. Environ. Prot. Agency.

Cardwell, R.D., et al. 1977. Acute and chronic toxicity of chlordane to fish and invertebrates. EPA Ecol. Res. Ser., U.S. Environ. Prot. Agency, Duluth, Minn.

Clemens, H.P., and K.E. Sneed. 1959. Lethal doses of several commercial chemicals for fingerling channel catfish. U.S. Dept. Inter. Fish Wildl. Sci. Rep. No. 316, Sept.

Goodman, L., et al. 1978. Effects of heptachlor and toxaphene on laboratory-reared embryos and fry of the sheepshead minnow. Proc. 30th Annu. Conf. S.E. Assoc. Game Fish Comm.

Henderson, C., et al. 1959. Relative toxicity of ten chlorinated hydrocarbon insecticides to four species of fish. Trans. Am. Fish. Soc. 8: 23.

Katz, M. 1961. Acute toxicity of some organic insecticides to three species of salmonids and to the threespine stickleback. Trans. Am. Fish. Soc. 90: 264.

Korn, S., and R. Earnest. 1974. Acute toxicity of twenty insecticides to striped bass, Morone saxatilis Calif. Fish Game. 60: 128.

Lu, P.Y., et al. 1975. Evaluation of environmental distribution and fate of hexachlorocyclopentadiene, chlordene, heptachlor, and heptachlor epoxide in a laboratory model ecosystem. Jour. Agric. Food Chem. 23: 967.

Ludemann, D., and H. Neumann. 1960. Acute toxicity of modern contact insecticides to carp, Cyprinus carpio. Z. Agnew. Zool. 47: 11.

Ludemann, D., and H. Neumann. 1961. Acute toxicity of present contact insecticides for freshwater animals. Z. Agnew. Zool. 48: 87.

Ludemann, D., and H. Neumann. 1962. Action of modern insecticides on the organisms in freshwater. Anz. Schadlingskunde. 35: 5.

Macek, K.J., et al. 1969. The effects of temperature on the susceptibility of bluegills and rainbow trout to selected pesticides. Bull. Environ. Contam. Toxicol. 4: 174.

Malone, C. R., and B. G. Blaylock. 1970. Toxicity of insecticide formulations to carp embryos reared in vitro. Jour. Wildl. Manage. 34: 460.

Mayhew, J. 1955. Toxicity of seven different insecticides to rainbow trout Salmo gairdneri Richardson. Proc. Iowa Acad. Sci. 62: 599.

Mehrle, P.M., et al. 1974. Nutritional effects on chlordane toxicity in rainbow trout. Bull. Environ. Contam. Toxicol. 2: 513.

Morgan, W.S.G. 1975. Monitoring pesticides by means of changes in electric potential caused by fish opercular rhythms. Prog. Water Technol. (G.B.). 7: 33.

Moore, R., et al. 1977. Absorption and elimination of ^{14}C-alpha-and gamma-chlordane by a freshwater alga, daphnid, and goldfish. Arch. Environ. Contam. Toxicol. 6: 411.

Naqvi, S.M.Z. 1973. Toxicity of twenty-three insecticides to a tubificid worm Branchiura sowerbyi from the Mississippi delta. Jour. Econ. Ent. 66: 70.

Naqvi, S.M., and D.E. Ferguson. 1970. Levels of insecticide resistance in freshwater shrimp, Palaemonetes kadiakensis. Trans. Am. Fish. Soc. 4: 696.

Parrish, P.R., et al. 1976. Chlordane: Effects on several estuarine organisms. Jour. Toxicol. Environ. Health 1: 485.

Parrish, P.R., et al. 1978. Chronic toxicity of chlordane, trifluralin, and pentachlorophenol to sheepshead minnows (Cyprinodon variegatus). EPA Rep. No. EPA 600/3-78-010: 1. U.S. Environ. Prot. Agency.

Sanborn, J.R., et al. 1976. The fate of chlordane and toxaphene in a terrestrial-aquatic model ecosystem. Environ. Entomol. 5: 533.

Sanders, H.O. 1969. Toxicity of pesticides to the crustacean Gammarus lacustris. U.S. Dep. Inter. Fish Wildl. Tech. Pap. 25, January.

Sanders, H.O. 1972. Toxicity of some insecticides to four species of malacostracan crustaceans. U.S. Dep. Inter. Fish Wildl. Tech. Pap. 66, August.

Sanders, H.O., and O.B. Cope. 1968. The relative toxicities of several pesticides to naiads of three species of stoneflies. Limnol. Oceanogr. 13: 112.

Schimmel, S.C., et al. 1976a. Heptachlor: Toxicity to and uptake by several estuarine organisms. Jour. Toxicol. Environ. Health 1: 955.

Schimmel, S.C., et al. 1976b. Heptachlor: Uptake, depuration, retention and metabolism by spot, Leiostomus xanthurus (Pisces:Sciaenidae). Jour. Toxicol. Environ. Health 2: 169.

Summerfelt, R.C., and W.M. Lewis. 1967. Repulsion of green sunfish by certain chemicals. Jour. Water Pollut. Control Fed. 39: 2030.

U.S. Food and Drug Administration. 1977. Administrative Guidelines Manual 7426.04, Attachment D.

Mammalian Toxicology and Human Health Effects

EXPOSURE

Ingestion from Water

Ballinger (1978) reviewed the lowest detectable concentrations for a number of chemicals and concluded that the limit for chlordane is 1 µg/l for an analyst using standardized procedures, with 0.3 µg/l being the most sensitive detection level using more sophisticated techniques. By using unusually large quantities of sample and concentration measures, the sensitivity may be increased.

A study of the persistence of technical chlordane in river water showed 85 percent remaining after 8 weeks, (Eichelberger and Lichtenberg, 1971). Of the major components of technical chlordane, cis- and trans-chlordane were completely stable over the 8-week period. All but two of the remaining components were at least partially changed.

Schafer, et al. (1969), examined over 500 grab samples from water supplies of the Mississippi and Missouri Rivers. Chlordane was detected in over 20 percent of the finished waters, with the maximum concentration being 8 µg/l. An extensive search of the literature and U.S. EPA reports generated from the Agency's analytical activities resulted in a list of organic compounds in drinking water of the United States (U.S. EPA, 1975). The highest concentration reported for chlordane did not exceed that reported by Schafer, et al. (1969). Chlordane has also been detected in rainwater (Bevenue, et al. 1972; U.S. EPA, 1976).

Although reports occasionally are received of individual household wells becoming contaminated after a house is treated with chlordane for termite control, only one report has been pub-

lished of the contamination of a municipal water system (Harrington, et al. 1978). On March 24, 1976 a section of the public water system supplying 105 persons in Chattanooga, Tenn., became contaminated. Back siphonage apparently occurred while diluting a chlordane concentrate with a hose during a period of negative pressure. Of the 71 residents affected, 13 had symptoms of mild acute chlordane toxicity. None of the residents has had prolonged sequelae from the exposure.

Ingestion from Foods

The Food and Drug Administration (FDA) has been systematically monitoring chlordane in the food supply of the United States since 1965. Chlordane has been found infrequently during the 11 years of survey (Nisbet, 1976). The only quantifiable sample collected was 0.059 mg/kg measured in a sample of grain in 1972 (Manske and Johnson, 1975). In the most recent published results (for 1975) chlordane was not detected, even in trace amounts (Johnson and Manske, 1977). Nisbet (1976) discussed the problems of compositing and analytical methods. Residues of technical chlordane are multi-component, so that the practical detection limit is several times higher than the 0.003 mg/kg stated for single components. Using data from FDA and others, Nisbet calculated an average chlordane intake from fish of 1 µg/day and concluded that fish represent the most significant dietary exposure to chlordane.

A bioconcentration factor (BCF) relates the concentration of a chemical in water to the concentration in aquatic organisms, but BCF's are not available for the edible portions of all four major groups of aquatic organisms consumed in the United States. Since

data indicate that the BCF for lipid-soluble compounds is proportional to percent lipids, BCF's can be adjusted to edible portions using data on percent lipids and the amounts of various species consumed by Americans. A recent survey on fish and shellfish consumption in the United States (Cordle, et al. 1978) found that the per capita consumption is 18.7 g/day. From the data on the 19 major species identified in the survey and data on the fat content of the edible portion of these species (Sidwell, et al. 1974), the relative consumption of the four major groups and the weighted average percent lipids for each group can be calculated:

Group	Consumption (Percent)	Weighted Average Percent Lipids
Freshwater fishes	12	4.8
Saltwater fishes	61	2.3
Saltwater molluscs	9	1.2
Saltwater decapods	18	1.2

Using the percentages for consumption and lipids for each of these groups, the weighted average percent lipids is 2.3 for consumed fish and shellfish.

An average measured steady-state bioconcentration factor of 12,066 was obtained for chlordane in four studies with sheepshead minnows containing 5 percent lipids (Goodman, et al. 1976; Parrish, et al. 1976, 1978). An adjustment factor of 2.3/5.0 = 0.46 can be used to adjust the measured BCF from the 5.0 percent lipids of the sheepshead minnow to the 2.3 percent lipids that is the weighted average for consumed fish and shellfish. Thus, the weighted average bioconcentration factor for chlordane and the edible portion of all aquatic organisms consumed by American is calculated to be 12,000 x 0.46 = 5,500.

The National Academy of Sciences (1977) in reviewing the results of Moore (1975) reported that of 200 samples of milk collected in Illinois during the period 1971-1973, 87 percent were positive for chlordane. The average concentration was 50 µg/l. Cyclodienes, such as chlordane, apparently are ingested with forage and tend to concentrate in lipids. Oxychlordane, a major mammalian metabolite of chlordane and heptachlor, was found in 46 percent of 57 human milk samples collected during 1973-74 in Arkansas and Mississippi. The mean value was 5 µg/l and the maximum was 20 µg/l (Strassman and Kutz, 1977).

Inhalation

In a survey of the extent of atmospheric contamination by pesticides, air was sampled at nine localities representative of both urban and agricultural areas. At least one chlorinated pesticide was found at all locations but chlordane was not found in any samples (Stanley, et al. 1971). In a larger survey summarized by Nisbet (1976), 2,479 samples were collected at 45 sites in 16 states. Chlordane was detected in only two samples, with concentrations of 84 and 204 ng/m^3.

Dermal

Chlordane can be absorbed through the skin and produce toxic effects (Gosselin, et al. 1976). Dermal exposure would be expected to occur only with occupational manufacture or use of the pesticide. Absorption can range from negligible to that producing acute effects, depending on the degree of exposure. For the general population, dermal exposure would be negligible. Persons using chlordane could have the pesticide persist on their skin for long periods. In one study, hexane rinsings of the hands of a

former pest control operator contained chlordane 2 years after his last known exposure (Kazen, et al. 1974).

PHARMACOKINETICS

Absorption

Cis- and trans-chlordane are the primary components of the insecticide. Both are stable when held under ambient conditions or mixed with the feed of experimental animals. A single oral dose of chlordane administered to rats resulted in approximately 6 percent absorption (Barnett and Dorough, 1974). Small daily doses result in greater absorption of 10 to 15 percent. Feeding the pure cis- and trans-isomers separately indicates that the cis-isomer is more effectively eliminated from the rats than the trans-form. Although the difference is not extensive, the data indicate that in long-term exposure situations, trans-chlordane would contribute a relatively greater amount to the body burden of the exposed animal than would the cis-isomer.

Distribution

Barnett and Dorough (1974) also studied the distribution of chlordane and metabolites in rats, using radioactive carbon. The levels of residues in the tissues were generally low, except in the fat. Levels of chlordane residues in the fat of the rats, after being fed 1, 5, and 25 mg/kg in their diet for 56 days, were approximately three times the concentration in the diet. Concentrations in the liver, kidney, brain, and muscle were 12, 10, 4, and 2 percent, respectively, of the concentration in the feed.

Once the chlordane was removed from the diet, all residues declined steadily for 4 weeks at which time the concentrations were reduced about 60 percent. During the following 4 weeks, the

residues declined only slightly. Treatment with trans-chlordane resulted in higher concentrations of residues in the tissues than treatment with the cis-isomer.

Dorough and Hemken (1973) fed three levels of chlordane to cows for 60 days and tested the milk periodically. Milk levels of chlordane and the metabolite oxychlordane increased sharply the first week and more slowly thereafter. When chlordane was removed from the diet, the milk residues dropped rapidly during the week following termination of treatment and stabilized after 2 weeks.

Metabolism

Polen, et al. (1971) and Street and Blau (1972) found oxychlordane to be a mammalian metabolite of chlordane, and to persist in adipose tissue. Street and Blau (1972) observed that the toxicity of oxychlordane was greater than the parent compound. Barnett and Dorough (1974) tentatively identified several hydroxylated metabolites of chlordane in rat excreta in addition to oxychlordane and concluded that the metabolism of chlordane takes place via a series of oxidative enzyme reactions.

Tashiro and Matsumura (1977) attempted to isolate and positively identify the metabolic products from chlordane to establish the route of its metabolism. The major route of metabolism for both cis- and trans-chlordane is via dichlorochlordene and oxychlordane. These metabolic intermediates are further converted to two key metabolites, 1-exo-hydroxy-2-chlorochlordene and 1-exo-hydroxy-2-endo-chloro-2,3-exo-epoxychlordene, which are readily degraded further. Trans-chlordane is more readily metabolized through this route.

There is yet another major metabolic route for cis-chlordane which involves more direct hydroxylation reactions to form 1-exo-hydroxydihydrochlordenes and 1,2-trans-dihydroxydihydrochlordene. Cis-chlordane is more readily degraded through this latter route. As judged by a toxicity test on mosquito larvae, none of the metabolic end products appears to be more toxic than the original chlordanes or the intermediates.

Excretion

Most chlordane is excreted in the feces of rats. Only about 6 percent of the total intake is voided in the urine. Rabbits, however, provide a different pattern. Urinary elimination of chlordane in rabbits is greater than excretion in the feces. This suggests that the conjugative metabolism system is more efficient in rabbits than in rats. The patterns of excretion following inhalation of chlordane by rats follow the patterns reported for oral administration (Nye and Dorough, 1976).

Human half-life data were obtained when chlordane was accidently ingested by a young boy (Curley and Garrettson, 1969). A whole body value of 21 days was calculated, which is long compared to drugs used in therapy, but quite short when compared to other chlorinated insecticides. This compares to a half-life of about 23 days obtained by Barnett and Dorough (1974) in studies with rats fed chlordane for 56 days. After the levels reached 60 percent, further reduction was slight. Serum half-life of chlordane in a young girl was found to be 88 days by Aldrich and Holmes, (1969).

EFFECTS

Acute, Sub-acute, and Chronic Toxicity

Human toxicity data for chlordane usually is obtained after accidental exposure to the compound. Curley and Garrettson (1969) reported that shortly after a 20-month-old boy accidently drank an unknown amount of chlordane he vomited and began a series of convulsions lasting 3 to 5 minutes each. After being given 14 mg/kg body weight phenobarbital, the seizures stopped. Body temperature rose to 102°F and then gradually decreased to normal. At no time was there evidence of pulmonary disease. Neurological examination at the time seizures were occurring revealed brisk deep tendon reflexes in all extremities. Cranial nerve function was intact and nystagmus was absent. An EEG taken 48 hours after exposure was normal. Three months after exposure, all tests appeared normal. Similar cases were reported by Dadey and Krammer (1953) and Aldrich and Holmes (1969). Barnes (1967) reported that intermittent dermal exposure of a nursery worker to chlordane as a soil insecticide produced symptoms including repeated seizures, electroencephalographic dysrhythmia, convulsions, and twitching. After cessation of contact with chlordane, all symptoms disappeared.

Purified chlordane at a concentration of 100 ug/l was reported to induce cytotoxic effects in human HeLa cell cultures by inhibiting growth and altering cell morphology (Gabliks, 1965).

A number of studies have been conducted to determine chlordane LD50 values for laboratory animals. Claude, et al. (1976) reported the oral LD50 of chlordane to be 350 mg/kg in rats, 390 mg/kg in mice, and 1,720 mg/kg in hamsters. Studies by Harbison (1975) showed the intraperitoneal LD50 of analytical chlordane to

be 343 mg/kg for the adult rat, 1,121 mg/kg for newborn rats and 539 mg/kg for newborn rats pretreated with 40 mg/kg sodium phenobarbital. Ben-Dyke, et al. (1970) reported an oral LD50 value of 283 mg technical grade chlordane/kg body weight for the rat. Ambrose, et al. (1953) reported a chlordane oral LD50 value of 590 mg/kg for the rat. Daily oral doses of 25 mg/kg or less for 15 days produced no toxic symptoms.

A review of the literature by the National Institute for Occupational Safety and Health (1976) indicated a range of chlordane LD50 values from 100 mg/kg for rabbits with oral administration to 700 mg/kg for rats with dermal administration. Gaines (1960) reported technical grade chlordane oral LD50 values of 335 mg/kg for male rats and 430 mg/kg for females and a dermal LD50 of 530 mg/kg for the female rat. The National Academy of Sciences (1977) reported dermal LD50 values of 840 and 690 mg/kg for male and female rats, respectively. Chlordane fed to rats at 2.5 mg/kg in the diet caused slight liver damage.

Wazeter, et al. (1968) reported acute oral LC50 values of 392 mg/kg, 327 mg/kg, and 371 mg/kg for cis-(alpha) chlordane, trans-(gamma) chlordane, and an equal mixture of the two isomers, respectively, in the male rat. Thus, the data indicate that technical grade chlordane and the individual purified chlordane isomers exhibit approximately equal toxicity. Boyd and Taylor (1969) observed that chlordane toxicity is increased in rats fed low protein diets. Oral LD50 values for reference grade technical chlordane ranged from 137 mg/kg for rats fed a low protein diet to 311 mg/kg for rats fed a normal protein diet.

Mice receiving 0.075 and 0.15 mg of cis- or trans-chlordane on days 2, 3, and 4 of life exhibited a delay in general maturation (Talamantes and Jang, 1977). Chlordane administered at 25 to 75 mg/kg in the Indian desert gerbil produced hyperglycemia and lowered the glucose tolerance, indicating an impairment in the uptake and utilization of glucose (Saxena and Karel, 1976). Repeated doses of 2.5 mg/kg chlordane to these animals produced changes in serum proteins, blood glucose, and alkaline and acid phosphatase activity (Karel and Saxena, 1976). The no-effect level, as indicated by induction of microsomal liver enzymes in male rats receiving chlordane in their diets over 2 weeks, was 5 mg/kg (Den Tonkelaar and Van Esch, 1974).

Hyde and Falkenberg (1976) studied neuroelectrical disturbances in rats as a result of injections of chlordane. Intraperitoneal injection of 350 mg/kg resulted in mild tremors and disorientation within a few minutes and death in 1 hour. Daily injection of 0.15, 1.75, and 25 mg/kg in adult rats resulted in dose-dependent alterations of brain potentials without behavioral signs of chronic toxicity. Changes were directly related to length of exposure, indicating that chlordane may be a cumulative neurotoxin.

Mammalian metabolism of the chlordane isomers results in the formation of the toxic metabolite oxychlordane (Street and Blau, 1972; Barnett and Dorough, 1974). Oxychlordane has been demonstrated to be approximately 20 times more toxic than the parent compound, with an acute oral LD50 value of approximately 19 mg/kg in male and female rats (Mastri, et al. 1969). Furthermore, oxychlordane has been demonstrated to be the most persistent metabo-

lite stored in rat adipose tissue (Street and Blau, 1972). The other products of chlordane isomer metabolism in rats are much less toxic (Mastri, et al. 1969).

Synergism and/or Antagonism

Histologic slides prepared from rats pretreated with 25 mg/kg chlordane and then injected with 0.5 ml of a 25 percent solution of carbon tetrachloride in olive oil revealed more extensive hepatocellular necrosis in the chlordane-pretreated rats than was found in the carbon tetrachloride treatment alone (Stenger, et al. 1975).

Ludke (1976) found that quail treated with chlordane followed by endrin had considerably more chlordane residues in their brains than did birds treated with chlordane alone, suggesting an increased uptake of chlordane in brains experiencing toxic effects from endrin exposure. Quail pretreated with 10 mg/kg chlordane exhibited decreased susceptibility (antagonism) to parathion but not to paraoxon dosage as measured by cholinesterase activity (Ludke, 1977).

Teratogenicity

Chlordane was found not to be teratogenic in rats when fed at concentrations of 150 to 300 mg/kg in the diet during pregnancy (Ingle, 1952).

Mutagenicity

Arnold, et al. (1977) administered chlordane to Charles River CD-1 male mice in a single dose of 50 or 100 mg/kg. The males were subsequently mated with untreated female mice. No dominant lethal changes were produced in the progeny. Studies by Ahmed, et al. (1977) with the SV-40 transformed human fibroblast cell line VA-4 showed chlordane induced unscheduled DNA synthesis, indicating that chlordane is a potential mutagen. Metabolic activation

eliminated the induction of unscheduled DNA synthesis. Simmon, et al. (1977) found that neither pure cis-chlordane nor trans- chlordane were mutagenic in the Ames Salmonella microsome assay. Technical grade chlordane, however, was found to be mutagenic in Salmonella typhimurium strains TA 1535, TA 98 and TA 100. An S-9 liver activation mix did not enhance the mutagenic activity.

Carcinogenicity

A dose-dependent incidence of hepatocellular carcinoma in male and female strain B6C3F1 mice fed diets containing analytical grade chlordane was reported by the National Cancer Institute (1977) and the results of their investigation are summarized in Table 1. This bioassay of chlordane for possible carcinogenicity was conducted by Gulf South Research Institute under contract to the National Cancer Institute. The batch tested contained 71.7 percent cis-chlordane, 23.1 percent trans-chlordane, 0.3 percent heptachlor, 0.6 percent nonachlor, 1.1 percent hexachlorocyclopentadiene, 0.25 percent chlordene isomers, and 2.95 percent unspecified chlorinated compounds. The material was incorporated into the feed of B6C3F1 hybrid mice.

Groups of 50 mice of each sex at 35 days of age were administered the test material at two concentrations for 80 weeks and then observed for 10 weeks. Matched controls were used during the tests. Since similar bioassays were conducted on five other compounds, the results were also given for the pooled controls. Hepatocellular carcinoma showed a highly significant dose-related trend for the mice. Male mice fed a time-weighted average concentration of 56.2 mg/kg chlordane in the diet for 80 weeks exhibited an 87.8 percent (43/49) incidence of liver tumors compared with an 11.1

TABLE 1

Liver carcinomas in mice associated with the oral feeding of chlordane

	% Positive (No. Tested)[1]		% Positive (No. Tested)[2]	
Dose (ppm)	Male	Female	Male	Female
63.8		69(49)		
56.2	88(49)			
50			82(39)	70(37)
30.1		6(47)		
29.9	33(48)			
25			79(52)	64(50)
5			9(55)	0(61)
0(controls)	11(18)	0(19)	9(33)	0(45)
0(controls)[3]	18(92)	4(78)		

(1) National Cancer Institute, 1977
(2) Epstein, 1976
(3) Pooled controls consisted of matched controls combined with other untreated mice.

percent (2/18) incidence in matched male controls and an 18.5 percent (17/92) incidence in pooled male controls from other experiments. In the same investigation, males fed a time-weighted average concentration of 29.9 mg/kg chlordane in the diet for 80 weeks exhibited a 33.3 percent (16/48) incidence of liver tumors. In the same investigation, female mice fed a time-weighted average concentration of 63.8 mg/kg chlordane in the diet for 80 weeks exhibited a 69.8 percent (34/49) incidence of liver tumors as compared with a 0 percent (0/19) incidence in matched female controls and a 3.8 percent (3/78) incidence in pooled female controls from other experiments. Female mice fed a time-weighted average concentration of 30.1 mg/kg chlordane in the diet for 80 weeks exhibited a 6.4 percent (3/47) incidence of liver tumors.

Similar studies were conducted by Gulf South with the chlordane, using Osborne-Mendel strain rats. Groups of 50 rats of each sex were administered low or high concentrations for 80 weeks and then observed for 29 weeks. Time-weighted average doses used for the male rats were 203.5 and 407.0 mg/kg, while the female rats received 120.8 and 241.5 mg/kg. The effects of chlordane on body weights and other clinical signs indicated that the dosages used were near the maximum permissible. In contrast to findings with mice, hepatocellular carcinomas failed to appear at a significant rate of incidence in rats administered chlordane. Further, the number of lesions of the liver in rats did not become significant with the inclusion of nodular neoplasia or with the application of life-table adjustment to the data.

In another bioassay, the International Research and Development Corp. (IRDC), using Analytical Reference Standard Chlordane (Tech.), fed groups of 100 male and 100 female Charles River CD-1 mice dietary levels of 5.0, 25, and 50 mg/kg food. Feeding commenced at 6 weeks of age and continued for 18 months (Epstein, 1976). The IRDC reort, reviewed by Epstein, made no inference and drew no conclusion regarding carcinogenicity, in spite of its conclusion that chlordane induced a statistically significant increase of nodular hyperplasias in the 25 and 50 mg/kg groups. The report also notes an increased incidence of hepatomas in the male 5.0 and 25 mg/kg groups. Epstein also reviewed the data of Reuber, who conducted a histological reevaluation of the IRDC slides and found that most of the histological material designated by IRDC as nodules were in fact carcinomas of the liver. Reuber's diagnoses were corroborated by three other independent pathologists and are summarized in Table 1. Thus, chlordane was found to produce liver cancer in both sexes of two different strains of mice.

CRITERION FORMULATION

Existing Guidelines and Standards

The American Conference of Governmental Industrial Hygienists (1977) adopted a time-weighted average value of 0.5 mg/m^3 for chlordane based on inhalation exposure. The short-term exposure limit (15 minutes) was set at 2 mg/m^3.

An acceptable daily dose for man has been estimated to be 0.001 mg/kg body weight (Food Agric. Organ., 1968). Although a limit of 3 ug/l was originally suggested for chlordane under the proposed Interim Primary Drinking Water Standards (40 FR 11990, March 14, 1975), the final U.S. EPA regulations (40 FR 59566, December 24, 1975) did not include a limit in view of the cancellation proceedings under the Federal Insecticide, Fungicide, and Rodenticide Act (40 FR 59566, December 24, 1975). Canadian Drinking Water Standards (Dep. Natl. Health Welfare, 1968) list a tentative maximum permissible limit for chlordane of 3 ug/l, which is applicable to raw water supplies in Canada.

Levels of Exposure and Special Groups at Risk

Nisbet (1976) estimated total daily intake of chlordane from all possible sources by back-calculating from the level of oxychlordane stored in tissue. A value of 9 µg/day chlordane intake was obtained. Nisbet also identified highly exposed segments of the general population: children as a result of milk consumed; fishermen and their families because of the high consumption of fish and shellfish, especially freshwater fish; persons living downwind from treated fields; and persons living in houses treated with chlordane pesticide control agents.

Basis and Derivation of Criterion

Several approaches are available to estimate a criterion level for chlordane in ambient water. Using the Food and Agricultural Organization/World Health Organization value of 0.001 mg/kg of body weight as the maximum daily human intake, and assuming an average body weight of 70 kg, the allowable intake would be 70 µg/day. Further, subtracting Nisbet's (1976) value of 9 µg as the daily intake from fish, shellfish, milk, inhalation, etc., and assuming that the contribution from drinking water is a negligible part of this value, the ambient water criterion becomes 61 µg/day. At 2 liters per day consumption, the maximum allowable concentration would be 30 µg/l.

The proposed U.S. EPA drinking water regulations (40 FR 11990, March 14, 1975), the Canadian standards, and the National Technical Advisory Committee (Fed. Water Pollut. Control Admin., 1968) all suggest a chlordane limit of 3 µg/l for drinking water. The latter report specifically indicates that the water treatment process has little effect on chlordane.

Although there are limitations to the procedure, the industrial inhalation exposure limit of the American Conference of Governmental Industrial Hygienists (1977) may be converted to a limit for ingestion (Stokinger and Woodward, 1958). Assuming absorption via the GI tract for chlordane is one-fifth the absorption by inhalation:

$$\frac{0.5\ \text{mg}}{\text{m}^3} \times \frac{10\text{m}^3}{\text{workday}} \times \frac{5\text{d work week}}{7\text{d week}} \times \frac{1}{5} = 0.7\ \text{mg/day}$$

Consumption of 2 liters of water daily and the consumption of 18.7 grams of contaminated fish which have a bioconcentration factor of 5,500 result in a maximum permissible concentration of 6.7 µg/l for the ingested water.

The use of inhalation data assumes an 8-hour day, time-weighted average occupational exposure in the working place with workers inhaling the toxic substance throughout such a period. Exposures for the general population should be considerably less. Such worker-exposure inhalation standards are inappropriate for the general population since they presume an exposure limited to an 8-hour day, an age bracket of the population that excludes the very young and the very old, and a healthy worker prior to exposure. Ingestion data is superior to inhalation data when the risks associated with the food and water of the water environment are being considered.

Under the Consent Decree in NRDC v. Train, criteria are to state "recommended maximum permissible concentrations (including where appropriate, zero) consistent with the protection of aquatic organisms, human health, and recreational activities". Chlordane is suspected of being a human carcinogen. Because there is no recognized safe concentration for a human carcinogen, the recommended concentration of chlordane in water for maximum protection of human health is zero.

Because attaining a zero concentration level may be infeasible in some cases and in order to assist the Agency and States in the possible future development of water quality regulations, the concentrations of chlordane corresponding to several incremental lifetime cancer risk levels have been estimated. A cancer risk level provides an estimate of the additional incidence of cancer that may be expected in an exposed population. A risk of 10^{-5} for example, indicates a probability of one additional case of cancer for every 100,000 people exposed, a risk of 10^{-6} indicates one additional case of cancer for every million people exposed, and so forth.

In the Federal Register notice of availability of draft ambient water quality criteria, EPA stated that it is considering setting criteria at an interim target risk level of 10^{-5}, 10^{-6}, or or 10^{-7} as shown in the table below.

Exposure Assumptions (per day)	Risk Levels and Corresponding Criteria (1)			
	0	10^{-7}	10^{-6}	10^{-5}
2 liters of drinking water and consumption of 18.7 grams fish and shellfish. (2)	0	0.012 ng/l	0.12 ng/l	1.2 ng/l
Consumption of fish and shellfish only.	0	0.013 ng/l	0.13 ng/l	1.3 ng/l

(1) Calculated by applying a modified "one-hit" extrapolation model described in the Methodology Document to the animal bioassay data presented in Appendix I and in Table 1. Since the extrapolation model is linear at low doses, the additional lifetime risk is directly proportional to the water concentration. Therefore, water concentrations corresponding to other risk levels can be derived by multiplying or dividing one of the risk levels and corresponding water concentrations shown in the table by factors such as 10, 100, 1,000, and so forth.

(2) 98 percent of the chlordane exposure results from the consumption of aquatic organisms which exhibit an average bioconcentration potential of 5,500-fold. The remaining 2 percent of chlordane exposure results from drinking water.

Concentration levels were derived assuming a lifetime exposure to various amounts of chlordane, (1) occurring from the consumption of both drinking water and aquatic life grown in waters containing the corresponding chlordane concentrations and, (2) occurring solely from consumption of aquatic life grown in the waters containing the corresponding chlordane concentrations. Because data indicating other sources of chlordane exposure and their contributions to total body burden are inadequate for quantitative use, the figures reflect the incremental risks associated with the indicated routes only.

REFERENCES

Ahmed, F.E., et al. 1977. Pesticide induced DNA damage and its repair in cultured human cells. Mutat. Res. 42: 161.

Aldrich, F.D., and J.H. Holmes. 1969. Acute chlordane intoxication in a child. Arch. Environ. Health 19: 129.

Ambrose, A.M., et al. 1953. Pharmacological observations on chlordane. Fed. Proc. Am. Soc. Exp. Biol. 12: 298.

American Conference of Governmental Industrial Hygienists. 1977. TLVs thresholds limit values for chemical substances in workroom air adopted by ACGIH for 1977. Cincinnati, Ohio.

Arnold, D.W., et al. 1977. Dominant lethal studies with technical chlordane, HCS-3260, and heptachlor: heptachlor epoxide. Jour. Toxicol. Environ. Health 2: 547.

Ballinger, D.G. 1978. Personal communication.

Barnes, R. 1967. Poisoning by the insecticide chlordane. Med. Jour. Austr. 54: 972.

Barnett, J.R., and H.W. Dorough. 1974. Metabolism of chlordane in rats. Jour. Agric. Food Chem. 22: 612.

Ben-Dyke, R., et al. 1970. Acute toxicity data for pesticides (1970). Wildl. Rev. Pestic. Control 9: 119.

Bevenue, A., et al. 1972. Organochlorine pesticides in rainwater Oahu, Hawaii, 1971-72. Bull. Environ. Contam. Toxicol. 8: 238.

Boyd, E.M., and F.I. Taylor. 1969. The acute oral toxicity of chlordane in albino rats. Ind. Med. 38: 42.

Claude, J., et al. 1976. Use of the golden hamster in toxicology Lab. Anim. Sci. 26: 274.

Cordle, F., et al. 1978. Human exposure to polychlorinated biphenyls and polybrominated biphenyls. Environ. Health Perspect. 24: 157.

Curley, A., and L.K. Garrettson. 1969. Acute chlordane poisoning. Arch. Environ. Health 18: 211.

Dadey, J.L., and A.G. Krammer. 1953. Chlordane intoxication. Jour. Am. Med. Assoc. 153: 723.

Den Tonkelaar, E.M., and G.J. Van Esch. 1974. No-effect levels of organochlorine pesticides based on induction of microsomal liver enzymes in short-term toxicity experiments. Toxicology 2: 371.

Department of National Health and Welfare. 1968. Canadian drinking water standards and objectives. Ottawa.

Dorough, H.W., and R.W. Hemken. 1973. Chlordane residues in milk and fat of cows fed HCS 3260 (high purity chlordane) in the diet. Bull. Environ. Contam. Toxicol. 10: 208.

Eichelberger, J.W., and J.J. Lichtenberg. 1971. Persistence of pesticides in river water. Environ. Sci. Technol. 5: 541.

Epstein, S.S. 1976. Carcinogenicity of heptachlor and chlordane. Sci. Total Environ. 6: 103.

Federal Water Pollution Control Administration. 1968. Water quality criteria: report of the National Technical Advisory Committee to the Secretary of the Interior. U.S. Government Printing Office, Washington, D.C.

Food and Agricultural Organization of the United Nations/World Health Organization. 1968. 1967 evaluation of some pesticide residues in food.

Gabliks, J. 1965. Responses of cell cultures to insecticides. II. Chronic toxicity and induced resistance. Proc. Soc. Exp. Biol. Med. 120: 168.

Gaines, T.B. 1960. The acute toxicity of pesticides to rats. Toxicol. Appl. Pharmacol. 2: 88.

Goodman, L., et al. 1976. Effects of heptachlor and toxaphene on laboratory-reared embryos and fry of the sheepshead minnow. Proc. 30th Annu. Conf. S.E. Assoc. Game Fish Comm.

Gosselin, R.E., et al. 1976. Clinical toxicology of commercial products. 4th ed. Williams and Wilkins Co., Baltimore, Md.

Harbison, R.D. 1975. Comparative toxicity of some selected pesticides in neonatal and adult rats. Toxicol. Appl. Pharmacol. 32: 443.

Harrington, J.M., et al. 1978. Chlordane contamination of a municipal water system. Environ. Res. 15: 155.

Hyde, K.M., and R.L. Falkenberg. 1976. Neuroelectrical disturbance as indicator of chronic chlordane toxicity. Toxicol. Appl. Pharmacol. 37: 499.

Ingle, L. 1952. Chronic oral toxicity of chlordane to rats. Arch. Ind. Hyg. Occup. Med. 6: 357.

Johnson, R.D., and D.D. Manske. 1977. Pesticide and other chemical residues in total diet samples (XI). Pestic. Monitor. Jour. 11: 116.

Karel, A.K., and S.C. Saxena. 1976. Chronic chlordane toxicity: effect on blood biochemistry of Meriones hurrianae Jerdon, the Indian desert gerbil. Pestic. Biochem. Physiol. 6: 111.

Kazen, C., et al. 1974. Persistence of pesticides on the hands of some occupationally exposed people. Arch. Environ. Health 29: 315.

Ludke, J.L. 1976. Organochlorine pesticide residues associated with mortality: additivity of chlordane and endrin. Bull. Environ. Contam. Toxicol. 16: 253.

Ludke, J.L. 1977. DDE increases the toxicity of parathion to coturnix quail. Pestic. Biochem. Physiol. 7: 28.

Manske, D.D., and R.D. Johnson. 1975. Pesticide residues in total diet samples (VIII). Pestic. Monitor. Jour. 9: 94.

Mastri, C., et al. 1969. Unpublished data. In 1970 evaluation of some pesticide residues in food. Food Agric. Org. United Nations/World Health Org.

Moore, S., III. 1975. Proc. 27th Illinois Custom Spray Operators Training School. Urbana.

National Academy of Sciences. 1977. Drinking water and health. Washington, D.C.

National Cancer Institute. 1977. Bioassay of chlordane for possible carcinogenicity. NCI-CG-TR-8.

National Institute for Occupational Safety and Health. 1976. Suspected carcinogens - subfile of the NIOSH registry of toxic effects of chemical substances. 2nd ed. NIOSH-77-149.

Nisbet, I.C.T. 1976. Human exposure to chlordane, heptachlor, and their metabolites. Contract WA-7-1319-A. U.S. Environ. Prot. Agency.

Nye, D.E., and H.W. Dorough. 1976. Fate of insecticides administered endotracheally to rats. Bull. Environ. Contam. Toxicol. 15: 291.

Parrish, P.R., et al. 1976. Chlordane: effects on several estuarine organisms. Jour. Toxicol. Environ. Health 1: 485.

Parrish, P.R., et al. 1978. Chronic toxicity of chlordane, trifluralin, and pentachlorophenol to sheepshead minnows (Cyprinoden variegatus). EPA Report No. EPA 600/3-78-010:1. U.S. Environ. Prot. Agency.

Polen, P.B., et al. 1971. Characterization of oxychlordane, animal metabolite of chlordane. Bull. Environ. Contam. Toxicol. 5: 521.

Saxena, S.C., and A.K. Karel. 1976. On effect of chlordane on the blood glucose and of glucose administration on the acute chlordane toxicity in Meriones hurrianae Jerdon, the Indian desert gerbil. Bull. Environ. Contam. Toxicol. 13: 493.

Schafer, M.L., et al. 1969. Pesticides in drinking water. Environ. Sci. Technol. 3: 1261.

Sidwell, V.D., et al. 1974. Composition of the edible portion of raw (fresh or frozen) crustaceans, finfish, and mollusks. I. Protein, fat, moisture, ash, carbohydrate, energy value, and cholesterol. Mar. Fish. Rev. 36: 21.

Simmon, V.F., et al. 1977. Mutagenic activity of chemicals identified in drinking water. Presented at 2nd Int. Conf. Environ. Mutagens, Edinburgh, Scotland, July 1977.

Stanley, C.W., et al. 1971. Measurement of atmospheric levels of pesticides. Environ. Sci. Technol. 5: 430.

Stenger, R.J., et al. 1975. Effects of chlordane preteatment on the hepatotoxicity of carbon tetrachloride. Exp. Mol. Pathol. 23: 144.

Stokinger, H.E., and R.L. Woodward. 1958. Toxicologic methods for establishing drinking water standards. Jour. Am. Water Works Assoc. 50: 515.

Strassman, S.C., and F.W. Kutz. 1977. Insecticide residues in human milk from Arkansas and Mississippi, 1973-74. Pestic. Monitor. Jour. 10: 130.

Street, J.E., and S.E. Blau. 1972. Oxychlordane: accumulation in rat adipose tissue on feeding chlordane isomers or technical chlordane. Jour. Agric. Food Chem. 20: 395.

Talamantes, F., and H. Jang. 1977. Effects of chlordane isomers administered to female mice during neonatal period. Jour. Toxicol. Environ. Health 3: 713.

Tashiro, S., and F. Matsumura. 1977. Metabolic routes of cis- and trans-chlordane in rats. Jour. Agric. Food Chem. 25: 872.

U.S. EPA. 1975. Preliminary assessment of suspected carcinogens in drinking water. Rep. to Congress. U.S. Environ. Prot. Agency.

U.S. EPA. 1976. Consolidated heptachlor/chlordane hearing. Fed. Regis. 41: 7552.

Wazeter, F.X., et al. 1968. Alpha chlordane, gamma chlordane, alpha-gamma chlordane. Comparative acute oral toxicity (LD50) in male albino rats. In 1970 evaluation of some pesticide residues in food. Food Agric. Org. United Nations/World Health Org.

Appendix I

Derivation of Criterion for Chlordane

The IRDC lifetime study of chlordane at 25 ppm in the diet of CD-1 mice resulted in liver carcinomas in males in 41 of 52 treated mice and in 3 of 33 controls, according to a re-analysis of slides by Dr. Reuber (CAG report). Using a fish bioconcentration factor of 5,500 the water concentration estimated to result in a lifetime risk of 10^{-5} is calculated from the extrapolation model using the following parameters:

$n_t = 41$	le = 78 weeks
$N_t = 52$	$d = 25 \times 10^{-6} \times 0.13 \times 10^{-6}$ mg food per day/kg body weight
$n_c = 3$	= 3.25 mg/kg/day
$N_c = 33$	w = 0.041 kg
Le = 78 weeks	L = 78 weeks
	F = 0.0187 kg
	R = 5,500

The result is that the water concentration corresponding to a lifetime risk of 10^{-5} is 1.2 nanograms/liter.